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US ser no 10/083,529

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IN THE UNITED STATES PATENT OFFICE

Appln serial No. 10/083,529
Applicant: U.N. Das
Title: A method of stabilizing and potentiating....

Docket No UND 99.02 D 1
Primary Exr: Alton Pryor
Group Art Unit 1616

Response to the Office Action mailed 4/19/2006

This is a response to the Office Action mailed on April 19, 2006, for which the 3 month deadline falls on July 19, 2006. The Examiner is thanked for withdrawing the rejections from applicant's response filed on January 30 2006.

Responsive to the Office action mailed April 19, 2006, attached is a proposed new page numbered 15a which, with the approval of the Examiner, may be introduced in response to the description-rejection. The proposed page 15a states that salt solutions of polyunsaturated fatty acids (**PUFAs**), such as for example, lithium salts of PUFAs are well known to those skilled in the art and may be procured from commercial sources. The **proposed** page 15a does not raise any new-matter issues.

35 USC 112-first paragraph rejection of claims 1-7, based on a written description requirement:

1. **The rejection** states: "The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art.....at the time the application was filed". The Examiner has stated that "The specification recites in paragraphs 45-49 salt solution mixture of polyunsaturated fatty acids and lithium salt solution of polyunsaturated fatty acids. The specification does not describe the ingredients that constitute the salt solutions, and the specification does not describe how to arrive at the lithium salt of polyunsaturated fatty acids."

Applicant's response: It is submitted that "to one skilled in the art", a salt solution of a polyunsaturated fatty acid (PUFA) or a lithium salt solution of a PUFA is very well known. There are many examples in published literature, of salts of PUFAs such as gamma-linolenic acid, and in particular, a lithium salt of gama-linolenic acid (another PUFA) for treatment of cancer, e.g., human carcinoma.
The attached **Exhibit A** contains 12 pages listing 12 examples of publicly available references in related literature describing regarding the use of salt solutions (including lithium and sodium salts) of a PUFA such as gamma-linolenic acid. The 12 examples of published literature include:

1. "In vivo and invitro biotransformation of the lithium salt of gamma-linolenic acid...." by de Antueno R. Elliot M et al, in Br J cancer 1997.

2. "The effects of n-6 polyunsaturated fatty acids ...." by Jiang WG, et al in Br J Cancer, 1998.

3. "Growth inhibitory effect of lithium gammalinolenate...." by Ravichandran D, et al, in Eur J cancer, 1998.

4. "Effect of lithium gamma-linolenate....." by Ravichandran D, et al, in Br J Surg, 1998.

5. "A preliminary study on intravenous infusion of sodium eicosapentaenoate" by Liu Y et al, in Drug Dev Ind Pharm, 2000.

6. "Comparative anti-mitotic effects of lithium gamma-linolenate...." by Seegers JC, et al , Department of Physiology, University of Pretoria, South Africa.

7. "An open-label phase.....using lithium gammalinolenate" by Fearon KC, et al, in Anticancer Res, 1996.

8. "**The** spermicidal activity.....polyunsaturated fatty acids and their sodium salts", by Wang JZ et al, (Chinese article) in Shengzi Yu Biyun, 1987.

9. "**Stimulation** of afferent nerve terminals....sodium salts of some long-chain fatty acids", by Orbach J, and Andrews WH, in PMID 4489893 of PubMed.

10. "**Lithium** gamma-linolenate-induced ....", by Kinchington D, et al, in FEBS Lett, 1993.

11. "The effect of lithium gamma-linolenate .....", by Kairemo KJ, et al in Pancreas, 1998.

12. "Comparative anti-mitotic effects of lithium gamma-linolenate....", by Seegers JC, et al, Department of Physiology, University of Pretoria, South Africa.

The attached **Exhibit B** contains 5 pages of information from the outfit called SIGMA-ALDRICH of St. Louis, MO, USA, from where salts of PUFAs, for example, sodium salt of Linoleic acid, may be procured. Other examples of suppliers may be found by those skilled in the art.

Since salt solutions of PUFAs including sodium and lithium salt solutions of PUFAs are known to those skilled in the art, applicant believes that references to lithium salt solution of PUFAs in the specification **as filed** are completely intelligible to one skilled in the art.

It is further submitted that independent claim1 recites a salt solution mixture of PUFA and one or more anti-angiogenic substances. The mixture is referred to in claim 1 as "a salt solution **mixture**" explicitly showing that there are **two** components in the salt solution mixture: the first being a salt solution of a PUFA, the second one being an anti-angiogenic substance. If the Examiner so prefers, the wording of claim 1 will be modified

to recite: mixture of a salt solution of PUFA, and one or more **anti-angiogenic substances**.

Independent claim 5 recites a method of treating a tumor.....comprising : injecting into the located artery, a mixture of at least (i) an oily lymphographic agent as a carrier containing one or more of **anti-angiogenic substances**, (ii) a lithium salt solution of at least one PUFA chose from.....". Independent claim 7 recites a method of treating a cancerous tumor using an oily lymphographic agent as a carrier for (i) for at least one PUFA chosen from a lithium salt..... (ii) a predetermined cancer drug and **anti-angiogenic substance(s)** mixed with PUFAs... , and administering by injecting into said cancerous tumor a predetermined quantity of the fatty acids, anti-cancer drug and predetermined anti-angiogenic substance in the oily lymphographic agent as a carrier.

It is noted that each of the independent claims 1, 5, and 7 recites **a salt solution of a PUFA as well as an anti-angiogenic substance.** It is also noted that the Examiner in his present rejection has apparently **not** made note of the **anti-angiogenic substance** (of which the examples given in the text as originally filed are ANGIOSTATIN and ENDOSTATIN).

As the courts have repeatedly reminded the USPTO: "The goal is to answer the question `What did applicants invent?'" In re Abele, 684 F.2d 902, 907, 214 USPQ 682, 687. Accord, e.g., Arrhythmia Research Tech. v. Corazonix Corp., 958 F.2d 1053, 1059, 22 USPQ2d 1033, 1038 (Fed. Cir.1992).

The present invention, as described at least in paragraphs 29 to 49 of the description, makes an effort to stabilize and potentiate the actions of **anti-angiogenic substances/molecules**. As clearly stated in paragraph 61 of the description, PUFAs or cisEFAs administered as a combination with anti-angiogenic substances using the invention, are better available to be taken up by the tumor cells. More particularly, the passage starting at line 26 in paragraph 57 of the description states " The fatty acids (PUFAs) may be present in physiologically acceptable form including but not limited to glycerides, esters, free acid, amides phospholipids or **salts**."

The description as filed at the time of the application, at least in paragraphs 56-61, by using terminology easily intelligible to one skilled in the art, provides examples and sufficient objective enablement of the invention as claimed, to a person who is skilled in the art. It is submitted that objective enablement in the present description as originally filed, satisfies the requirement in the first paragraph of 35 USC 112. According to the observation made in "In re Marzocchi et al. (CCPAQ 1971) 439 F2d 1220, 169 USPQ 367", whether the objective enablement is achieved by the use of illustrative examples or by broad terminology is of no importance. Notwithstanding, the description as a whole provides enablement and examples of administering the mixture of the salt solution of a PUFA along with other ingredients as recited in independent claims 1, 5 and 7.

It is believed accordingly that the foregoing description-rejection stating that **claims which employ salt solution mixture are neither described nor exemplified** is not warranted and should be rescinded.

2. The rejection further states that "To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that applicant was in possession of the claimed invention."

Applicant's response: Independent claim1 recites a salt solution mixture of PUFA and one or more anti-angiogenic substances. The mixture is referred to in claim 1 as "a salt solution mixture" explicitly showing that there are **two** components in the salt solution mixture: the first being a salt solution of a PUFA, the second one being an anti-angiogenic substance. Independent claim 5 recites a method of treating a tumor.....comprising : injecting into the located artery, a mixture of at least (i) an oily lymphographic agent as a carrier containing one or more of **anti-angiogenic substances,** (ii) a lithium salt solution of at least one PUFA chose from.....". Independent claim 7 recites a method of treating a cancerous tumor using an oily lymphographic agent as a carrier for (i) for at least one PUFA chosen from a lithium salt..... (ii) a predetermined cancer drug and **anti-angiogenic substance(s)** mixed with PUFAs... , and administering by injecting into said cancerous tumor a predetermined quantity of the fatty acids , anti-cancer drug and predetermined anti-angiogenic substance in the oily lymphographic agent as a carrier. It is noted that each of the independent claims 1, 5, and 7 recites **a salt solution of a PUFA as well as an anti-angiogenic substance.**

The present invention, as stated at least in paragraphs 29-49 of the description, intends to stabilize and potentiate the actions of known anti-angiogenic molecules. As clearly stated in paragraph 61 of the description, PUFAs or cisEFAs administered as a combination with anti-angiogenic substances using the invention, are better available to be taken up by the tumor cells. More particularly, the passage starting at line 26 in paragraph 57 of the description states " The fatty acids (PUFAs) may be present in physiologically acceptable form including but not limited to glycerides, esters, free acid, amides phospholipids or **salts**." The description as a whole, filed at the time of the application, and more particularly, at least in paragraphs 56-61, provides examples and sufficient objective enablement of the invention as claimed, to a person who is skilled in the art. Applicant believes accordingly that the written description as originally filed, taken as a whole, conveys with clarity to one skilled in the art, that the applicant was in possession of the invention as of the time of the application.

The foregoing description-rejection is therefore believed to be untenable and should be withdrawn.

3. The rejection further states that with respect to claims 1-4, the claims recite "a salt solution mixture", which is inappropriate since a solution is a mixture.

Applicant's response: The claim 1 wording recites "a salt solution **mixture** of PUFA and one or more anti-angiogenic substances". The mixture is referred to in claim 1 as "a

salt solution **mixture**" explicitly showing that there are **two** components in the salt solution **mixture**: the first being a **salt solution** of at least one polyunsaturated fatty acid (PUFA), the second one being one or more anti-angiogenic substance(s).

If the Examiner so prefers, applicant is willing to modify the terminology in claim 1 to recite: "mixture of a salt solution of at least one polyunsaturated fatty acid in the form of a salt solution of at least one polyunsaturated fatty acid chosen from....., and one or more **anti-angiogenic substances"**. It is submitted that this suggested terminology-amendment in claim 1 may be done by an Examiner's amendment if such is acceptable.

In conclusion, in view of the foregoing clarifications and analysis, applicant believes that the 35 USC 112 rejection of the description does not apply and should be rescinded.

Also, with respect to the 35 USC 112 rejection of the claim 1 terminology, the term "a salt solution mixture" in claim 1 is explained hereinabove, and it is believed that the 35 USC 112 rejection in this respect does not apply. Notwithstanding, the passage including the term "mixture" in claim 1 but may be modified to read "mixture of a salt solution of at least one polyunsaturated fatty acid in the form of a salt solution of at least one polyunsaturated fatty acid chosen from....., and one or more **anti-angiogenic substance(s)"** as stated above, by an Examiner's amendment if it is acceptable to the Examiner. The examiner is requested to call the undersigned at **215 661 1140**, if a telephone call will be conducive to advance the prosecution to completion.

In view of the foregoing discussion and analysis, applicant believes that the 35 USC 112 rejection of the written description and the claims as on file is untenable, and that the claims 1-7 do particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

A favorable reconsideration of the application by rescinding the 35 USC 112 rejection, and a notice of allowance of all the claims 1-7 is earnestly requested.

Respectfully submitted,

Rama B Nath

Registration nr. 27,072

[0045a] A salt solution of a polyunsaturated fatty acid (PUFA) or a lithium salt solution of a PUFA is very well known in literature to those skilled in the art. There are many examples in published literature, of salts of PUFAs such as gamma-linolenic acid, and in particular, a sodium salt or a lithium salt of gamma-linolenic acid (another PUFA) for treatment of cancer, e.g., human carcinoma. Salts and salt solutions of PUFAs and related substances, for example, sodium salt of linolenic acid, may be procured commercially from SIGMA-ALDRICH of St. Louis, MO, USA. Other examples of suppliers of the PUFA salts and salt solutions may be found by those skilled in the art.

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ADDITIONAL PAGE